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Terms	Documents
Little-melvyn.in. or Kipriyanov-sergey.in. or moldenhauer-gehard.in.	6

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Search History

Today's Date: 5/2/2001

DB Name	Query	Hit Count	Set Name
USPT	Little-melvyn.in. or Kipriyanov-sergey.in. or moldenhauer-gehard.in.	6	L4
USPT	OKT3.clm.	20	L3
USPT	OXT3.clm.	0	L2
USPT	5852177.pn.	1	L1

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      (FILE 'HOME' ENTERED AT 08:18:23 ON 02 MAY 2001)

      FILE 'MEDLINE' ENTERED AT 08:18:40 ON 02 MAY 2001
L1          2923 S OKT3
L2        187545 S CYSTEINE OR STABIL?
L3            26 S L1 AND L2

=> s little m/au
L4           176 LITTLE M/AU

=> s l4 and l1
L5             2 L4 AND L1
```

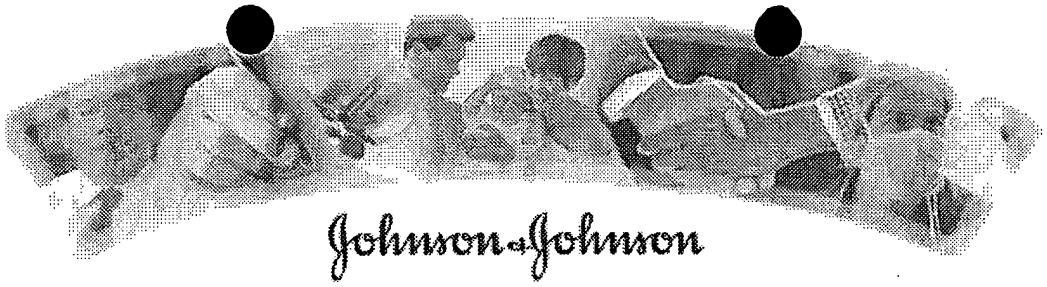
L3 ANSWER 5 OF 26 MEDLINE

ACCESSION NUMBER: 97337430 MEDLINE
DOCUMENT NUMBER: 97337430 PubMed ID: 9194170
TITLE: Two amino acid mutations in an anti-human CD3 single chain Fv antibody fragment that affect the yield on bacterial secretion but not the affinity.
AUTHOR: Kipriyanov S M; Moldenhauer G; Martin A C; Kupriyanova O A;
Little M
CORPORATE SOURCE: Department of Molecular Immunology, German Cancer Research Center (DKFZ), Heidelberg, Germany.
SOURCE: PROTEIN ENGINEERING, (1997 Apr) 10 (4) 445-53.
Journal code: PR1; 8801484. ISSN: 0269-2139.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970902
Last Updated on STN: 19970902
Entered Medline: 19970818

AB Recombinant antibody fragments directed against cell surface antigens have facilitated the development of novel therapeutic agents. As a first step in the creation of cytotoxic immunoconjugates, we constructed a single-chain Fv fragment derived from the murine hybridoma **OKT3**, that recognizes an epitope on the epsilon-subunit of the human CD3 complex. Two amino acid residues were identified that are critical for the high level production of this scFv in Escherichia coli. First, the substitution of glutamic acid encoded by a PCR primer at position 6 of VH framework 1 by glutamine led to a more than a 30-fold increase in the production of soluble scFv. Second, the substitution of **cysteine** by a serine in the middle of CDR-H3 additionally doubled the yield of soluble antibody fragment without any adverse effect on its affinity for the CD3 antigen. The double mutant scFv (Q,S) proved to be very stable in vitro: no loss of activity was observed after storage for 1 month at 4 degrees C, while the activity of scFv containing a **cysteine** residue in CDR-H3 decreased by more than half. The results of production yield, affinity, **stability** measurements and analysis of three-dimensional models of the structure suggest that the sixth amino acid influences the correct folding of the VH domain, presumably by affecting a folding intermediate, but has no effect on antigen binding.

L3 ANSWER 1 OF 26 MEDLINE
ACCESSION NUMBER: 2001178458 MEDLINE
DOCUMENT NUMBER: 21099443 PubMed ID: 11169443
TITLE: Recombinant chimeric **OKT3** scFv IgM antibodies mediate immune suppression while reducing T cell activation in vitro.
AUTHOR: Choi I; De Ines C; Kurschner T; Cochlovius B; Sorensen V; Olafsen T; Sandlie I; Little M
CORPORATE SOURCE: Recombinant Antibody Research Group (D0500), German Cancer Research Center, Heidelberg, Germany.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (2001 Jan) 31 (1) 94-106.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: Germany: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered PubMed: 20010222
Entered Medline: 20010329

AB **OKT3**, a mouse anti-human CD3 monoclonal antibody (mAb), is a potent immunosuppressive agent used in clinical transplantation to treat allograft rejection. Two major drawbacks of this therapy are the systemic release of several cytokines due to cross-linking mediated by the mAb between T cells and FcgammaR-bearing cells and the human anti-mouse antibody (HAMA) response. To overcome these side effects, three chimeric **OKT3** single chain variable fragment (scFv) IgM antibodies, scOKT3-gamma DeltaIgM wt, scOKT3-gamma DeltaIgM C575S and scOKT3-gamma DeltaIgM VAEVD, were generated. They consist of the light and heavy variable binding domains of **OKT3** mAb as well as the CH3 and CH4 domains of different human IgM variants linked with a human IgG3 hinge region to provide more flexibility and **stability**. Like the native IgM, scOKT3-gamma DeltaIgM antibodies are able to form polymeric structures, which lead to an increase in binding affinity and immunosuppressive potential compared with the parental **OKT3** mAb. However, independently of their polymerization, all scOKT3-gamma DeltaIgM constructs do not induce any significant T cell proliferation or cytokine release (IL-2, TNF-alpha and IFN-gamma) in in vitro assays, while their CD3-modulating properties are retained. These results suggest that the use of scOKT3-gamma DeltaIgM antibodies may offer significant advantages over the **OKT3** mAb in improving clinical immunosuppressive treatment



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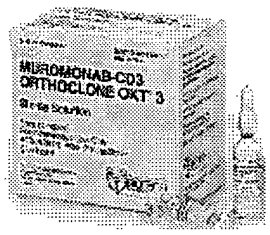

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Word Mark	**ORTHOCLONE** OKT
Goods and Services	IC 005. US 018. G & S: MONOCLONAL ANTIBODIES FOR IN VIVO THERAPEUTIC USE. FIRST USE: 19860725. FIRST USE IN COMMERCE: 19860725
Mark Drawing Code	(1) TYPED DRAWING
Serial Number	73617455
Filing Date	August 28, 1986
Published for Opposition	February 17, 1987
Registration Number	1438912
Registration Date	May 12, 1987
Owner	(REGISTRANT) JOHNSON & JOHNSON CORPORATION NEW JERSEY ONE JOHNSON & JOHNSON PLAZA NEW BRUNSWICK NEW JERSEY 089337001
Attorney of Record	MICHAEL J. RYAN, JR.
Prior Registrations	1199209;1204190
Type of Mark	TRADEMARK
Register	PRINCIPAL
Affidavit Text	SECT 15. SECT 8 (6-YR).
Live/Dead Indicator	LIVE

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Typed Drawing

Word Mark	**ORTHOCLONE**
Goods and Services	IC 005. US 018. G & S: Monoclonal Antibody Used as Therapeutic Agent in Immune Deficient Disease States. FIRST USE: 19810611. FIRST USE IN COMMERCE: 19810611
Mark Drawing Code	(1) TYPED DRAWING
Serial Number	73337989
Filing Date	November 19, 1981
Published for Opposition	December 14, 1982
Registration Number	1229215
Registration Date	March 8, 1983
Owner	(REGISTRANT) JOHNSON & JOHNSON CORPORATION NEW JERSEY ONE JOHNSON & JOHNSON PLAZA NEW BRUNSWICK NEW JERSEY 089337001
Attorney of Record	RICHARD F. BIRIBAUER
Prior Registrations	1199209
Type of Mark	TRADEMARK
Register	PRINCIPAL
Affidavit Text	SECT 15. SECT 8 (6-YR).
Live/Dead Indicator	LIVE

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Word Mark	OKT
Goods and Services	IC 001. US 006. G & S: In Vitro Reagents for Laboratory Use-Namely, Monoclonal Antibodies Used to Determine Patient's Immunity to Disease. FIRST USE: 19800225. FIRST USE IN COMMERCE: 19800225
Mark Drawing Code	(1) TYPED DRAWING
Serial Number	73257550
Filing Date	April 10, 1980
Published for Opposition	May 18, 1982
Registration Number	1204190
Registration Date	August 10, 1982
Owner	(REGISTRANT) Johnson & Johnson CORPORATION NEW JERSEY 501 George St. New Brunswick NEW JERSEY 08903
Attorney of Record	RICHARD F. BIRIBAUER
Type of Mark	TRADEMARK
Register	PRINCIPAL
Affidavit Text	SECT 15. SECT 8 (6-YR).
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1: Chadd HE, Chamow SM. Relate

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Curr Opin Biotechnol. 2001 Apr;12(2):188-94.
PMID: 11287236 [PubMed - in process]

2: Little M, Kipriyanov SM, Le Gall F, Moldenhauer G. Relate

Of mice and men: hybridoma and recombinant antibodies.
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3: Boel E, Verlaan S, Poppelier MJ, Westerdaal NA, Van Strijp JA, Logtenberg T. Relate

Functional human monoclonal antibodies of all isotypes constructed from phage displa library-derived single-chain Fv antibody fragments.
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PMID: 10821956 [PubMed - indexed for MEDLINE]